Female Sexual Dysfunction in ESRD: An Underappreciated Epidemic?

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While life-sustaining, chronic dialysis is associated with substantial impairments in health-related quality of life (HRQoL) (1,2). The well-recognized decrements in HRQoL in patients with ESRD are likely related to multiple factors, including functional limitations, impaired social well being, vocational disruptions associated with a thrice-weekly or quotidian treatment, and a large burden of physical and emotional symptoms. Specific symptoms that occur with regularity in patients on chronic dialysis are fatigue, cramping, pain, and dyspnea (3,4). Another symptom that appears to occur frequently in patients with ESRD is sexual dysfunction, etiologies for which include hormonal dysregulation, vascular disease, autonomic dysfunction, medication side effects, and psychologic illness such as depression (5,6).

To date, the preponderance of research on sexual dysfunction in patients with ESRD has focused on men. Although there are several domains of male sexual function that may be impaired, the most frequently studied has been erectile dysfunction (ED), in part because of the availability of efficacious pharmacological therapy (7,8). Multiple studies have documented ED to be highly prevalent and strongly correlated with HRQoL in men on chronic dialysis and have identified the clinical predictors of this symptom (9,10). In a comprehensive cross-sectional study of 302 community-based male hemodialysis patients, Rosas *et al.* (9,11) found that ED was present in 82%, was severe in 45%, and was associated with impairments in multiple domains of HRQoL. A subsequent study by Türk *et al.* (10) demonstrated that ED was present in 104 (70%) of 148 patients on chronic hemodialysis and was closely correlated with decrements in physical and mental well being. Older age and diabetes were associated with ED in both of these studies. Data from these and other studies, which collectively enrolled thousands of patients, confirm the high prevalence and clinical importance of ED in men on dialysis and inform our understanding of factors that help predict the presence of this symptom.

Although women comprise approximately one-half of all patients with ESRD, considerably less attention has been paid to female sexual dysfunction in this population. A series of small past studies suggest that sexual dysfunction is common among women receiving chronic dialysis. Yazici *et al.* (12) studied 117 women with ESRD and found that sexual dysfunction was present in 94% of patients on peritoneal dialysis and 100% of those on hemodialysis. More recently, Seethala *et al.* (13) found impairments in multiple domains of sexual function in 66 female patients on chronic dialysis and high rates of sexual dysfunction among women with partners and those who reported to be sexually active. Notwithstanding these findings, studies investigating this issue were limited by the enrollment of small numbers of patients and the lack of statistical power to elucidate which clinical factors are associated with and predict the presence of sexual dysfunction.

In an effort to broaden our understanding of the prevalence and correlates of female sexual dysfunction in ESRD, in this issue of *CJASN*, Strippoli (14) report the results of a large study of women receiving chronic hemodialysis. In this cross-sectional analysis, 1472 women were recruited from 27 randomly selected dialysis units in Europe and South America and asked to complete the Female Sexual Function Index (FSFI), a commonly used 19-item instrument that assesses six discrete domains of sexual function over the previous 4 weeks: desire, arousal, lubrication, orgasm, satisfaction, and pain. The maximum score for each domain is 6, and a composite summary score is generated by summing individual domain scores. Summary scores range from 2.0 to 36, with lower scores indicating more severe sexual dysfunction and a score <26.55 denoting the presence of sexual dysfunction (15). In addition to administering the FSFI, the investigators collected comprehensive demographic and clinical data and asked patients to complete the Center for Epidemiologic Studies-Depression instrument to assess for depression. Recursive partitioning and amalgamation was used to delineate groups of clinical variables that correlated with the presence of sexual dysfunction.

Overall, 659 of 1472 women (45%) completed the study questionnaires. Among these 659 participants, 555 (84%) were identified as having sexual dysfunction based on FSFI scores <26.55. Individual domains with the greatest level of dysfunction were arousal (median, 1.8), orgasm (median, 2.0), and desire (median, 2.4), whereas satisfaction (median, 3.6) appeared to be the least impaired domain. In adjusted analyses, factors associated with a lower risk for sexual dysfunction included having a partner or being listed for a kidney transplant, whereas symptoms of depression, lower

educational levels, menopausal status, diabetes as a cause of ESRD, and use of a diuretic were independently associated with greater risk for sexual dysfunction. Recursive partitioning and amalgamation analyses demonstrated that women without partners who were not wait-listed for a kidney transplant were at the highest risk for sexual dysfunction (adjusted odds ratio, 21.91; 95% confidence interval, 9.99–48.04). Of the 362 women with a partner, 282 (79%) had sexual dysfunction. Slightly more than one-third of patients ($n=232$) reported being sexually active, of whom 128 (55%) had FSFI scores consistent with sexual dysfunction. Among these women, depression, menopausal status, low serum albumin, and diuretic therapy were associated with greater risk for sexual dysfunction.

This comprehensive study by Strippoli is one of the largest and, arguably, most methodologically robust analysis to date of sexual dysfunction in women on hemodialysis, demonstrating that this symptom appears to be remarkably common among women and that specific demographic and clinical variables may predict risk. Notwithstanding the large and diverse study population and statistically sound analyses, several caveats, many of which were raised in the article, should be considered when interpreting this study's results and drawing conclusions that could inform clinical care. First, more than one-half ($n=813$) of all enrolled patients did not complete and return the FSFI, and a greater proportion of these subjects were older, had reached menopause, were not living with a partner, and were not wait-listed for kidney transplant than patients who were included in the analyses. The inability to include such women may have contributed to an underestimation of the prevalence of sexual dysfunction overall and among specific subgroups of patients. Moreover, refusal of such a large proportion of patients to participate in what appears to be a low-risk, low-burden study raises questions about how women on dialysis perceive the issue of sexual function and whether the findings are broadly generalizable. Second, although the FSFI has been shown to be psychometrically sound and has been used previously in the ESRD population, certain features of its design impact its interpretation. Specifically, multiple items on the FSFI include the option for patients to indicate "no sexual activity," which is considered as a score of 0 on a 0–5 Likert scale. However, the absence of sexual activity does not necessarily reflect sexual dysfunction (16). Inclusion of scores of 0 in the calculation of FSFI scores may result in overestimation of the prevalence of sexual dysfunction. Therefore, the reported rate of sexual dysfunction in this study (84%) may be considerably greater than the true prevalence. To their credit, the investigators described their findings among the subgroup of women who reported being sexually active during the prior 4 weeks, demonstrating that a considerably lower, yet still notable, 55% of such patients had FSFI-defined sexual dysfunction. Third, it is important to note that the presence of sexual dysfunction based on FSFI scores does not necessarily signify dissatisfaction with one's sex life, as alluded to by the authors. This was well characterized in a study of 164 nonrenal patients by Ferenidou *et al.* (17), in which nearly 50% of women in a stable relationship met FSFI criteria for sexual dysfunction, yet >70% of these women with FSFI-defined sexual dysfunction reported satisfaction with their sexual function based on responses on the Symptom Checklist of Sexual Function survey. It seems possible that a reasonable proportion of female dialysis patients with FSFI-defined sexual dysfunction would also report being satisfied with their sexual function. Finally, the current study did not assess whether sexual dysfunction was treated in study participants or if patients noted to have this symptom desired treatment. Unlike phosphodiesterase-5 inhibitors for men with ED, there is a pronounced dearth of evidence-based, effective treatment options for sexual dysfunction among women on chronic dialysis. It is also interesting to note that just 35% of women who completed study surveys reported being sexually active. Although the absence of a partner may explain this finding in part, a dyadic relationship is certainly not a prerequisite for sexual activity. Whether sexual dysfunction is the primary explanation for the low proportion of sexually active women on dialysis is not entirely clear from the present study; this question certainly warrants further investigation.

Although it is premature to label sexual dysfunction as an epidemic among women receiving chronic hemodialysis, this study by Strippoli sheds important light on this symptom and its correlates. Future efforts to determine how many women on dialysis with sexual dysfunction perceive distress from this symptom and which patients are interested in considering treatment is an important first step toward developing and testing treatment interventions that could potentially improve specific domains of sexual function, as well as the overall well being and quality of life of this chronically ill patient group.

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Disclosures

None.

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